

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference K 3195	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/EP2004/011269	International filing date (day/month/year) 08/10/2004	(Earliest) Priority Date (day/month/year) 10/10/2003
Applicant DEUTSCHES KREBSFORSCHUNGSZENTRUM STIFTUNG DES...		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 10 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box II).

3. ☒ **Unity of invention is lacking** (see Box III).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☒ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2004/011269

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☐ contained in the international application as filed
 - ☐ filed together with the international application in computer readable form
 - ☒ furnished subsequently to this Authority for the purpose of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/011269

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 13-18
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-20 (partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 13-18

Present claims 13-18 relate to an extremely large number of possible compounds/products, namely to any activator/agonist, inhibitor/antagonist or binding partner of a futrin. These compounds are defined merely by being obtainable via the methods of claims 1-12 of the present application. However, neither the claims nor the description of the present application disclose any structural features of these compounds. Thus, claims 13-18 are considered to lack clarity within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT to an extent that a meaningful search over the whole or even over a part of the claimed scope is impossible.

Consequently, no search has been carried out for claims 13-18.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-20 (partially)

Diagnostic compositions involving / diagnostic uses of futrin 1 nucleic acid molecules, peptides or ligands; method of diagnosing a disease associated with aberrant expression or activity of futrin 1; method of identifying and obtaining a drug candidate for therapy of such a disease; method for identifying binding partners to / (ant)agonists of futrin 1; use of a futrin 1 activity-encoding nucleotide molecule, a futrin 1-polypeptide, an activator/agonist of a futrin 1 polypeptide or binding partner thereof for the preparation of a pharmaceutical composition for activating or inhibiting the Wnt signal cascade.

2. claims: 1-20 (partially)

Diagnostic compositions involving / diagnostic uses of futrin 2 nucleic acid molecules, peptides or ligands; method of diagnosing a disease associated with aberrant expression or activity of futrin 2; method of identifying and obtaining a drug candidate for therapy of such a disease; method for identifying binding partners to / (ant)agonists of futrin 2; use of a futrin 2 activity-encoding nucleotide molecule, a futrin 2-polypeptide, an activator/agonist of a futrin 2 polypeptide or binding partner thereof for the preparation of a pharmaceutical composition for activating or inhibiting the Wnt signal cascade.

3. claims: 1-20 (partially)

Diagnostic compositions involving / diagnostic uses of futrin 3 nucleic acid molecules, peptides or ligands; method of diagnosing a disease associated with aberrant expression or activity of futrin 3; method of identifying and obtaining a drug candidate for therapy of such a disease; method for identifying binding partners to / (ant)agonists of futrin 3; use of a futrin 3 activity-encoding nucleotide molecule, a futrin 3-polypeptide, an activator/agonist of a futrin 3 polypeptide or binding partner thereof for the preparation of a pharmaceutical composition for activating or inhibiting the Wnt signal cascade.

4. claims: 1-20 (partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Diagnostic compositions involving / diagnostic uses of futrin 4 nucleic acid molecules, peptides or ligands; method of diagnosing a disease associated with aberrant expression or activity of futrin 4; method of identifying and obtaining a drug candidate for therapy of such a disease; method for identifying binding partners to / (ant)agonists of futrin 4; use of a futrin 4 activity-encoding nucleotide molecule, a futrin 4-polypeptide, an activator/agonist of a futrin 4 polypeptide or binding partner thereof for the preparation of a pharmaceutical composition for activating or inhibiting the Wnt signal cascade.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/011269

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/060942 A (INCYTE GENOMICS, INC; WARREN, BRIDGET, A; HONCHELL, CYNTHIA, D; LU, YA) 8 August 2002 (2002-08-08)	1-12
A	abstract; claims 1-87 page 10, line 16 - page 15, line 12	19,20
X	& DATABASE GENESEQ 5 November 2002 (2002-11-05), retrieved from EMBL Database accession no. ABG76508	1-12
A	abstract	19,20
X	----- WO 03/029405 A (HYSEQ, INC; TANG, Y., TOM; NUVELO) 10 April 2003 (2003-04-10)	1-12
A	abstract page 3, line 31 - page 8, line 14 claims 1-7	19,20
	-/--	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

11 May 2005

Date of mailing of the international search report

23.08.2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Madlener, M

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/011269

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	& DATABASE GENESEQ 18 August 2003 (2003-08-18), retrieved from EMBL Database accession no. ABR62106	1-12
A	abstract	19,20
X	----- WO 03/004676 A (APPLERA CORPORATION; CECCARDI, TONI; KETCHUM, KAREN; LADUNGA, ISTVAN) 16 January 2003 (2003-01-16)	1-12
A	abstract page 3, line 30 - page 4, line 5 claims 1-23	19,20
X	& DATABASE G 7 August 2003 (2003-08-07), retrieved from EMBL Database accession no. AAE37115	1-12
A	abstract	19,20
P,X	----- KAMATA TOMOYUKI ET AL: "R-spondin, a novel gene with thrombospondin type 1 domain, was expressed in the dorsal neural tube and affected in Wnts mutants." BIOCHIMICA ET BIOPHYSICA ACTA, vol. 1676, no. 1, 5 January 2004 (2004-01-05), pages 51-62, XP002326104 ISSN: 0006-3002 abstract page 60, right-hand column, paragraph 2 page 61	1-12,19, 20
A	----- CHEN JIN-ZHONG ET AL: "Cloning and identification of a cDNA that encodes a novel human protein with thrombospondin type I repeat domain, hPWTSR." MOLECULAR BIOLOGY REPORTS, vol. 29, no. 3, September 2002 (2002-09), pages 287-292, XP002326105 ISSN: 0301-4851 cited in the application the whole document	1-12,19, 20
A	----- BRANTJES HELEN ET AL: "TCF: Lady Justice casting the final verdict on the outcome of Wnt signalling." BIOLOGICAL CHEMISTRY. FEB 2002, vol. 383, no. 2, February 2002 (2002-02), pages 255-261, XP002326402 ISSN: 1431-6730 the whole document	19,20
	----- -/--	

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/011269

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>ES VAN J H ET AL: "You Wnt some, you lose some: Oncogenes in the Wnt signaling pathway" CURRENT OPINION IN GENETICS & DEVELOPMENT, CURRENT BIOLOGY LTD, vol. 13, no. 1, 20 February 2003 (2003-02-20), pages 28-33, XP002249368 ISSN: 0959-437X the whole document</p>	19,20
A	<p>BIENZ M ET AL: "Linking colorectal cancer to Wnt signaling" CELL, CELL PRESS, CAMBRIDGE, NA, US, vol. 103, 13 October 2000 (2000-10-13), pages 311-320, XP002174510 ISSN: 0092-8674 cited in the application the whole document</p>	19,20
A	<p>PEIFER M ET AL: "Wnt signaling in oncogenesis and embryogenesis-a look outside the nucleus" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 287, no. 5458, 3 March 2000 (2000-03-03), pages 1606-1609, XP002240707 ISSN: 0036-8075 cited in the application the whole document</p>	19,20
A	<p>GILES R H ET AL: "Caught up in a Wnt storm: Wnt signaling in cancer" BBA - REVIEWS ON CANCER, ELSEVIER SCIENCE BV, AMSTERDAM, NL, vol. 1653, no. 1, 5 June 2003 (2003-06-05), pages 1-24, XP004427852 ISSN: 0304-419X the whole document</p>	19,20
T	<p>KAZANSKAYA OLGA ET AL: "R-Spondin2 is a secreted activator of Wnt/beta-catenin signaling and is required for Xenopus myogenesis." DEVELOPMENTAL CELL. OCT 2004, vol. 7, no. 4, 11 October 2004 (2004-10-11), pages 525-534, XP009046814 ISSN: 1534-5807 the whole document</p>	1-12,19,20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/011269

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02060942	A	08-08-2002	CA 2434953 A1	08-08-2002
			EP 1356028 A2	29-10-2003
			JP 2005503108 T	03-02-2005
			WO 02060942 A2	08-08-2002
			US 2005142600 A1	30-06-2005

WO 03029405	A	10-04-2003	US 2003032034 A1	13-02-2003
			US 6783969 B1	31-08-2004
			CA 2458818 A1	10-04-2003
			EP 1427747 A2	16-06-2004
			JP 2005503821 T	10-02-2005
			WO 03029405 A2	10-04-2003
			AU 2002366951 A1	09-07-2003
			CA 2469941 A1	03-07-2003
			EP 1504099 A2	09-02-2005
			WO 03054152 A2	03-07-2003
			CA 2440257 A1	12-09-2002
			EP 1381621 A2	21-01-2004
			WO 02070539 A2	12-09-2002
			US 2004053250 A1	18-03-2004
			US 2004005592 A1	08-01-2004

WO 03004676	A	16-01-2003	US 2003022217 A1	30-01-2003
			CA 2449875 A1	16-01-2003
			EP 1501536 A2	02-02-2005
			WO 03004676 A2	16-01-2003
